Optum Health Education™

Evidence-Based COPD Management for the PCP

Curtis Sather, MD, FACCP
Senior Medical Director, Optum West

January 29, 2025

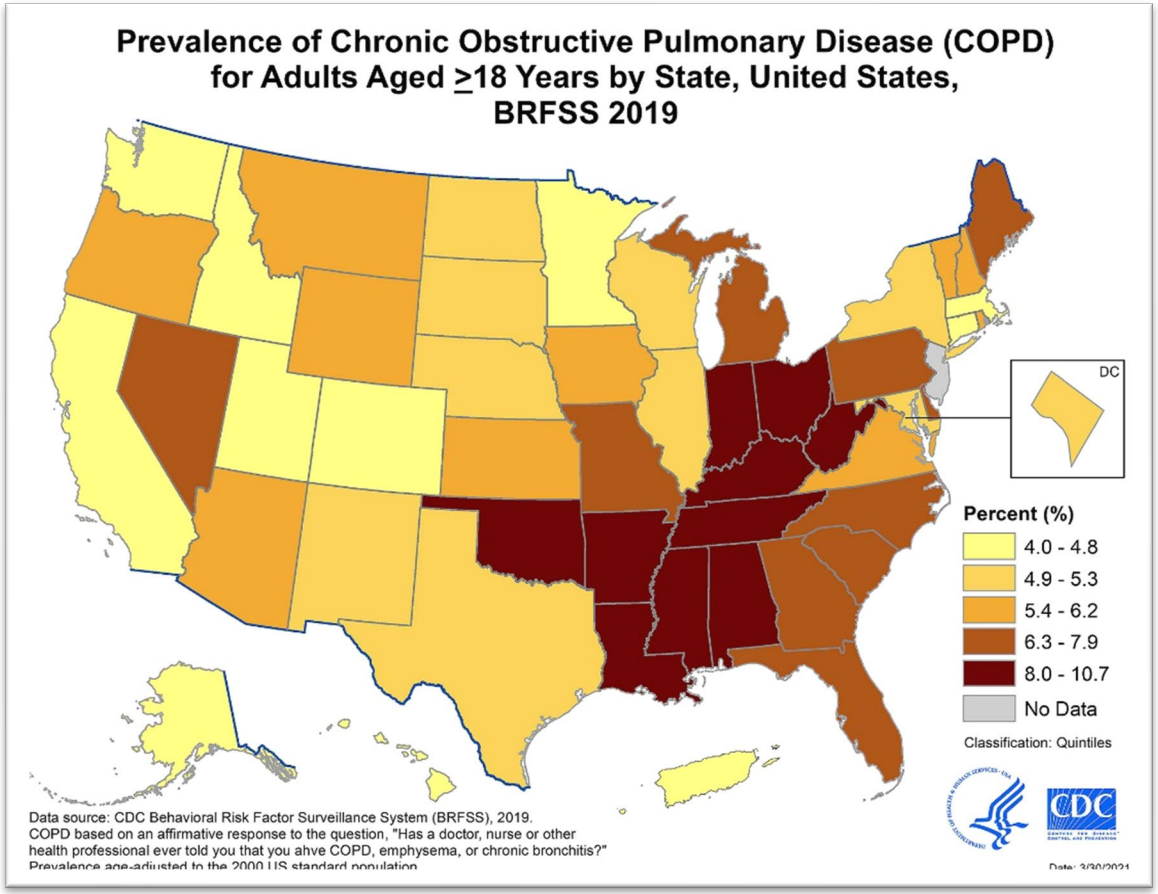
Learning Objectives

Upon completion of this activity, participants should be able to:

- Review the indications and potential harms of inhaled corticosteroid use in patients with COPD.
- Explain the indications and value considerations for recently approved medications for COPD patients.
- Describe parameters for identifying appropriate patients for treatment with supplemental oxygen.
- Discuss the benefits and implementation of pulmonary rehabilitation for COPD patients.
- Identify strategies to effectively counsel COPD patients on the benefits of vaccinations.

COPD epidemiology and impact

- 13 million in US have a dx of COPD – *underdiagnosed*!
- **Fourth-ranked cause of death in the United States**, killing more than 120,000 individuals each year.
- **Third leading cause worldwide** (and increasing).



- Likelihood of underdiagnosis Black >> non-Hispanic white.
- Female smokers that visit a physician are 1/3 less likely than men to be dx with COPD than male smokers.

COPD definition

COPD is a common, preventable, and treatable disease characterized by **persistent respiratory symptoms** and **airflow limitation**… usually caused by significant exposure to noxious particles or gases and influenced by host factors.

The "O" in COPD stands for Obstruction. **Demonstration of obstruction (FEV1/FVC <0.7) with spirometry** is necessary for a true COPD dx.

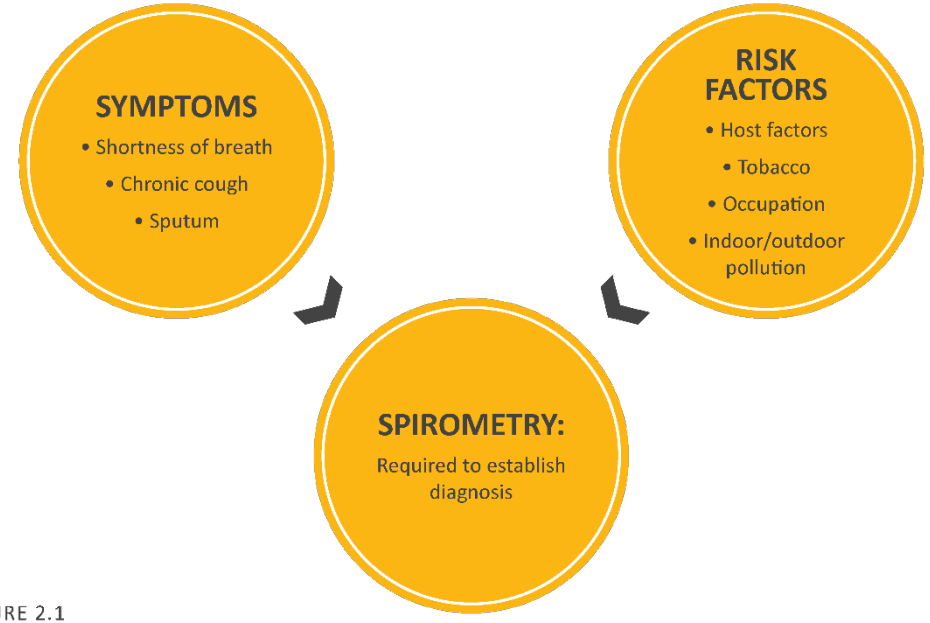


FIGURE 2.1

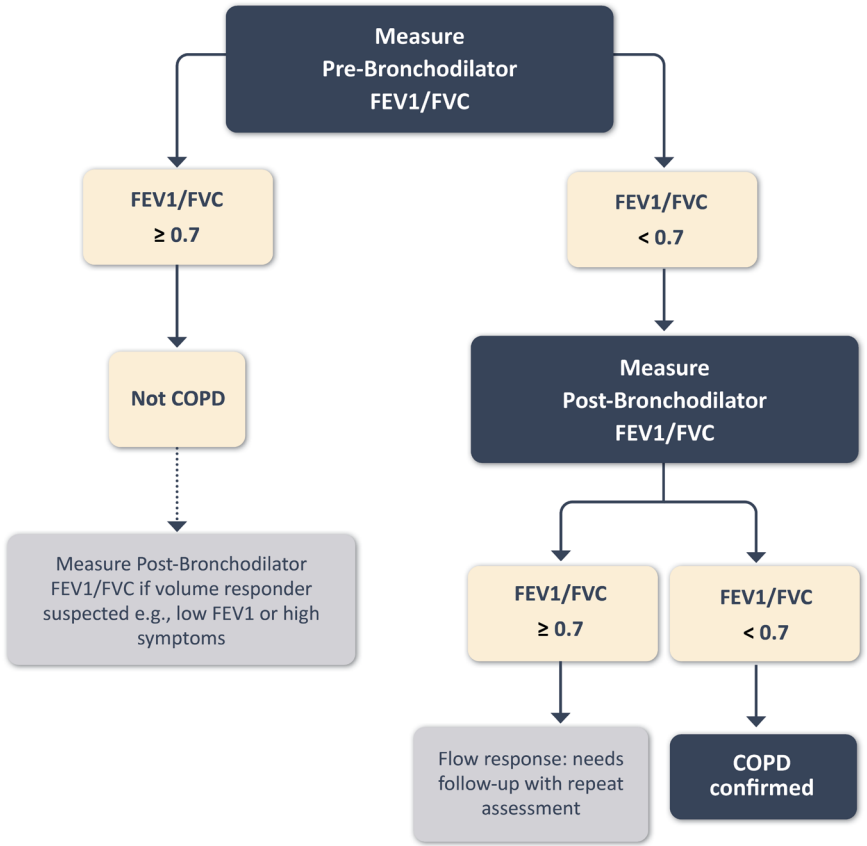
Spirometry is REQUIRED to diagnose COPD

However:

- Only ~32% of new COPD diagnoses in the US have had spirometry two years pre-dx to six months post-dx.
- 60% office setting, 40% hospital pulmonary function lab

Spirometry Utilization for COPD
Han, MeiLan K. et al. CHEST, Volume 132, Issue 2, 403 - 409

Pre- and Post- Bronchodilator Spirometry Figure 2.6

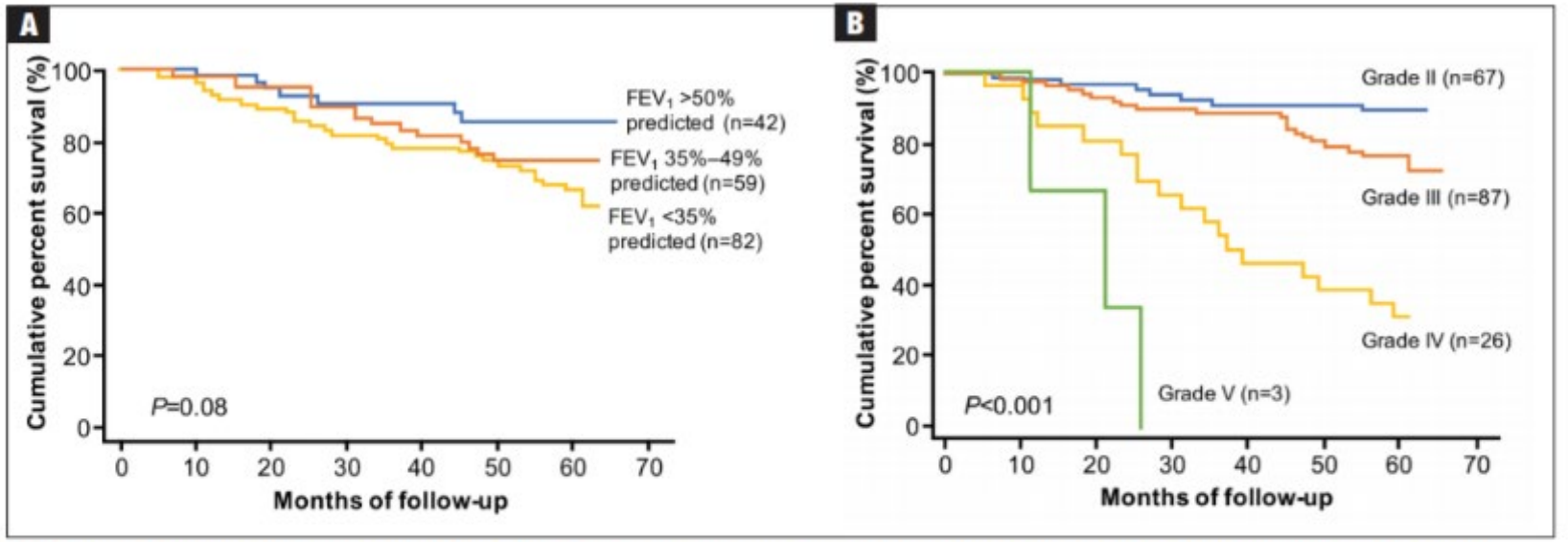


You've confirmed the diagnosis of COPD with spirometry.

What are the most important things to ask your patient?

Dyspnea – Why do we care?
It's a better predictor of mortality than lung function.

FIGURE 3 **Five-year survival according to (A) percentage of predicted FEV_1 and (B) dyspnea level[24]**



(A) Grades determined by 1995 American Thoracic Society staging guideline, which is categorized according to percentage of predicted FEV_1. (B) Grades determined by an adapted version of the Medical Research Council grading system (distinct from the modified Medical Research Council scale, which is used widely and cited in the GOLD report,[5] in which dyspnea is classified from Grade 0 to Grade 4), developed by Fletcher et al[25]: Grade I, I get breathless at times other than when doing strenuous exercise; Grade II, I am short of breath when hurrying on the level or walking up a slight hill; Grade III, I have to walk slower than most people on the level and I have to stop after a mile or so (or after 1/4 hour) on the level at my own pace; Grade IV, I have to stop for breath after walking about 100 yards (or after a few minutes) on the level; Grade V, I am too breathless to leave the house, or breathless after undressing.

Asking about dyspnea

"How short of breath are you?"

Asking about dyspnea

"How short of breath are you?"

"What activities cause you to be short of breath?"

"How long can you walk at a normal pace before needing to stop to catch your breath?"

Modified MRC Dyspnea Scale

Figure 2.9

PLEASE TICK IN THE BOX THAT APPLIES TO YOU | ONE BOX ONLY | Grades 0 - 4

mMRC Grade 0	mMRC Grade 1	mMRC Grade 2	mMRC Grade 3	mMRC Grade 4
I only get breathless with strenuous exercise	I get short of breath when hurrying on the level or walking up a slight hill	I walk slower than people of the same age on the level because of breathlessness, or I have to stop for breath when walking on my own pace on the level	I stop for breath after walking about 100 meters or after a few minutes on the level	I am too breathless to leave the house or I am breathless when dressing or undressing
☐	☐	☐	☐	☐

Reference: ATS (1982) Am Rev Respir Dis. Nov;126(5):952-6.

Exacerbation risk assessment

COPD exacerbations are defined as an acute worsening of respiratory symptoms that result in additional therapy.

Classified as:

- **Mild** (treated with SABDs only)
- **Moderate** (treated with SABDs plus antibiotics and/or oral corticosteroids)
- **Severe** (patient requires hospitalization or visits the emergency room).

History of exacerbation is the most important predictive factor for future exacerbations. (NOT severity of obstruction)

Asking about exacerbation history

"How many COPD exacerbations have you had?"

Asking about exacerbation history

"How many COPD exacerbations have you had?"

"Have you ever been to the ER for breathing problems?"

"How many times have you been prescribed steroid pills or antibiotics for breathing problems?"

"Low" exacerbation history

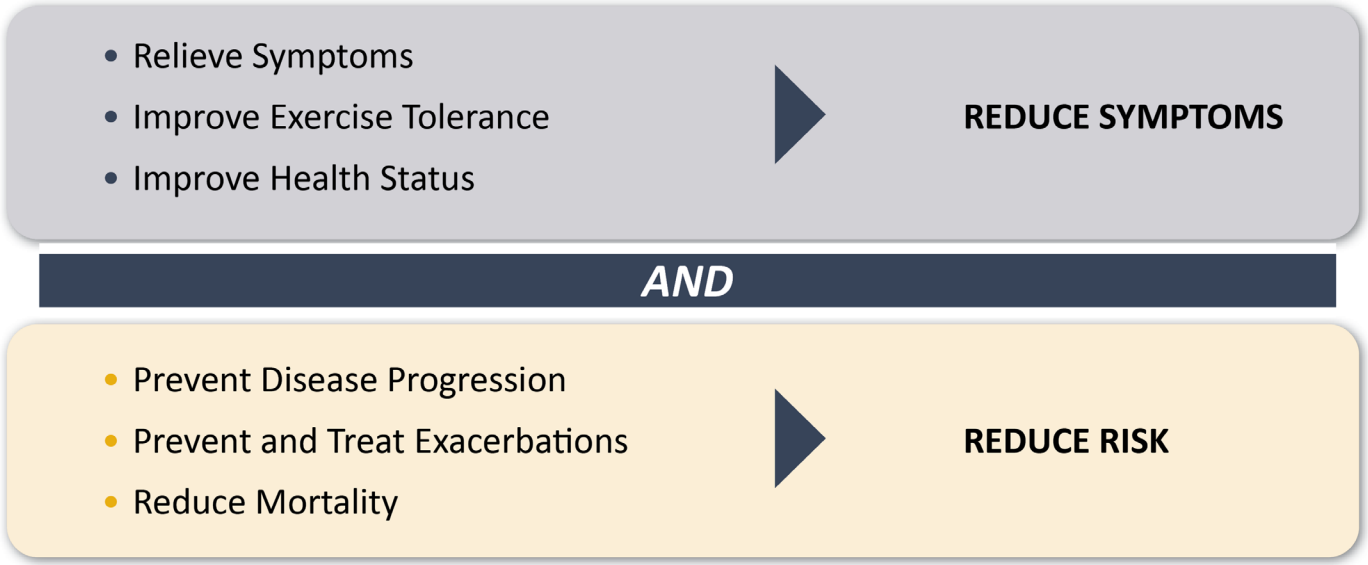
Zero to one
mod/severe exacerbations
(not leading to hospital admission)

"High" exacerbation history

Two or more
mod/severe exacerbations, OR
any leading to hospital admission

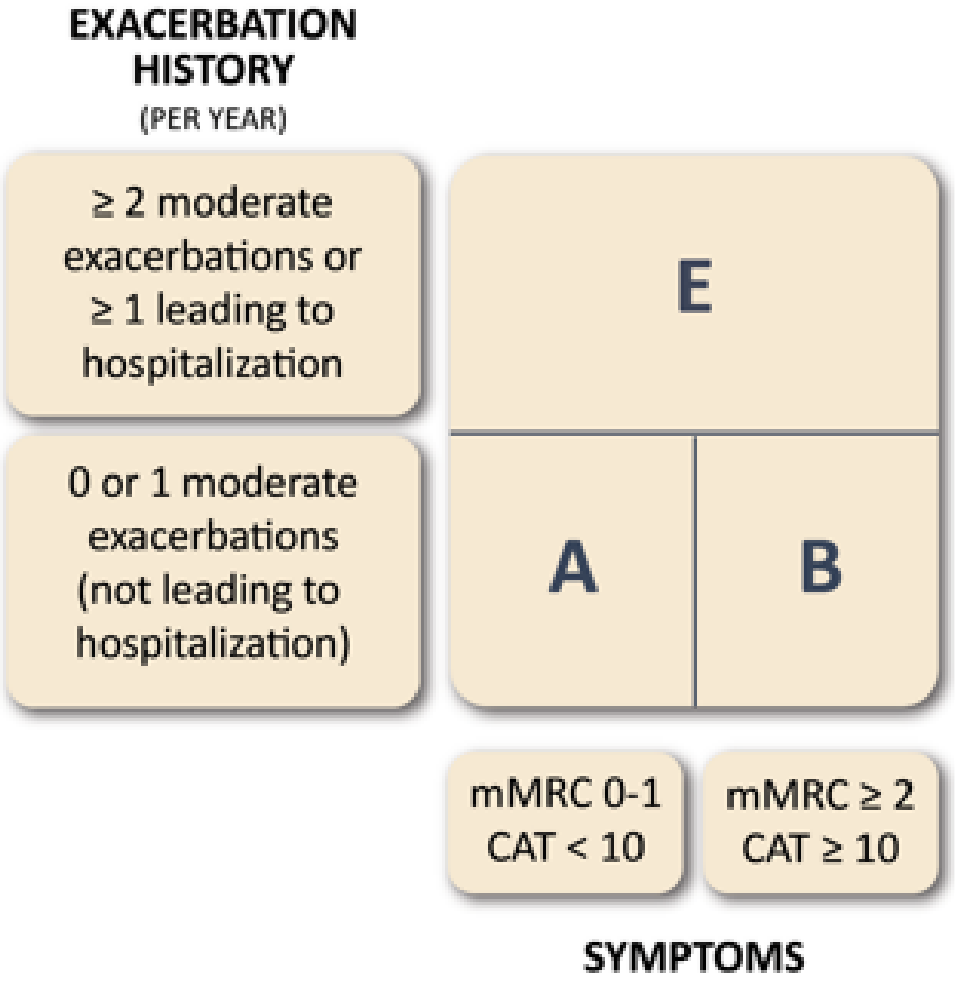
Goals for Treatment of Stable COPD

Figure 3.1



GOLD "ABE" Assessment Tool

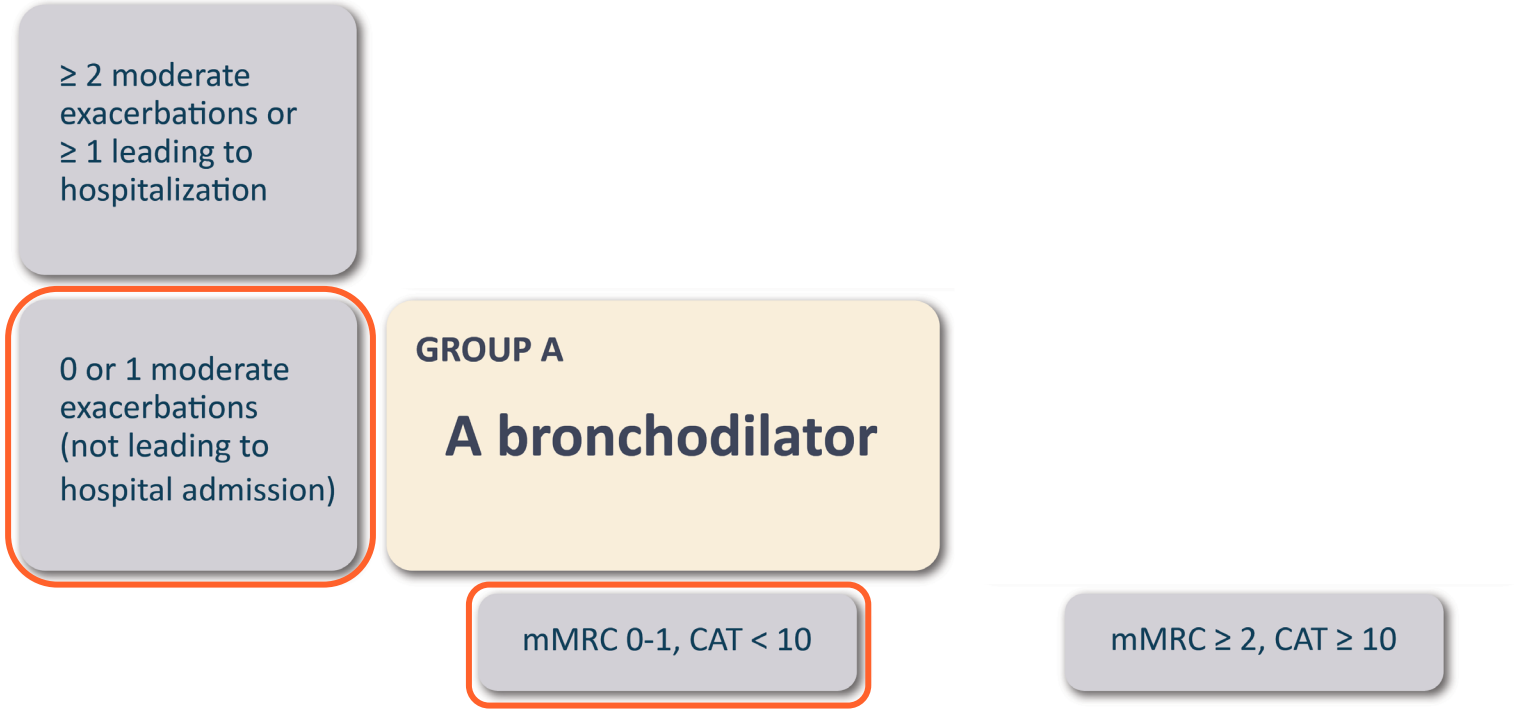
Assessing exacerbation hx and current sx will lead you to the right therapy.



How do I select the appropriate COPD maintenance therapy to initiate?

Initial Pharmacological Treatment

Figure 3.7

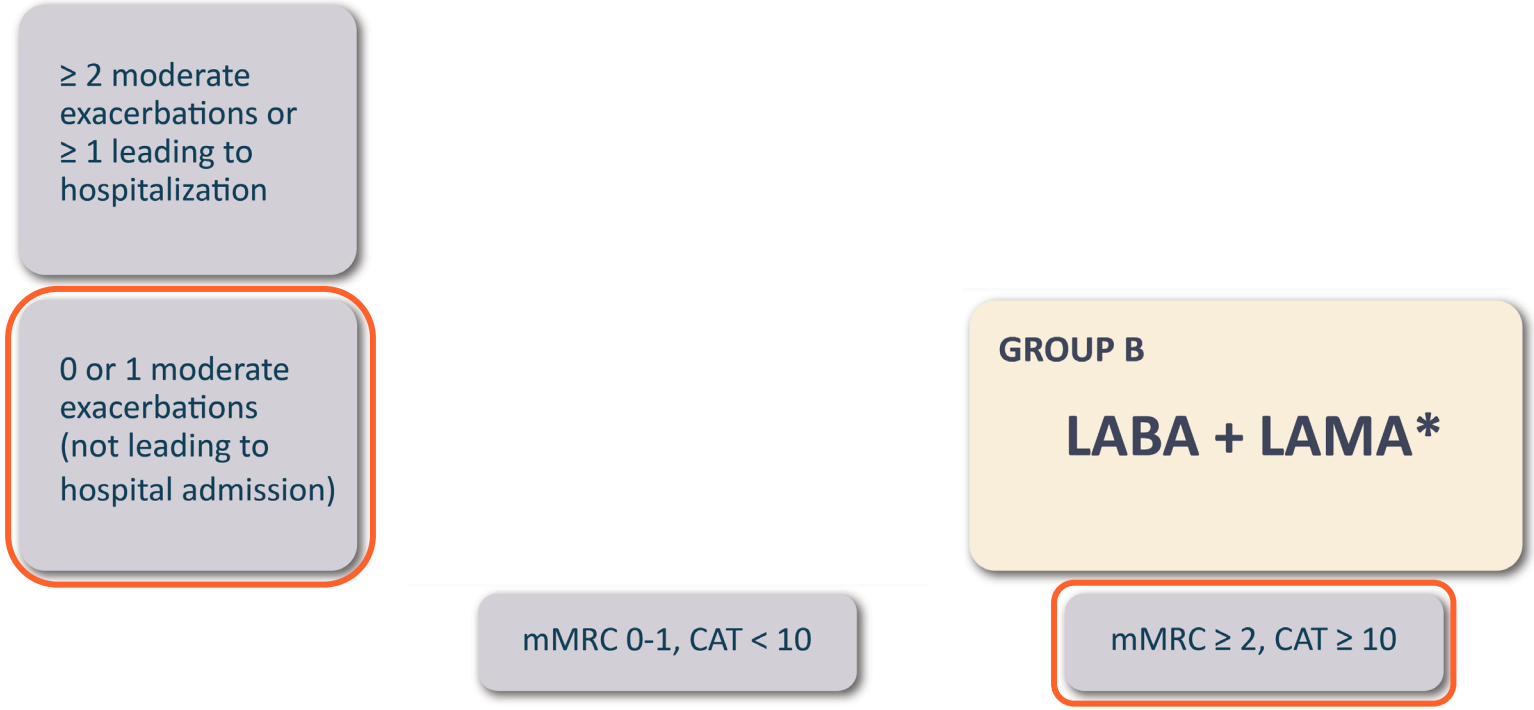


*Single inhaler therapy may be more convenient and effective than multiple inhalers; single inhalers improve adherence to treatment

Exacerbations refers to the number of exacerbations per year; eos: blood eosinophil count in cells per microliter; mMRC: modified Medical Research Council dyspnea questionnaire; CAT™: COPD Assessment Test™.

Initial Pharmacological Treatment

Figure 3.7

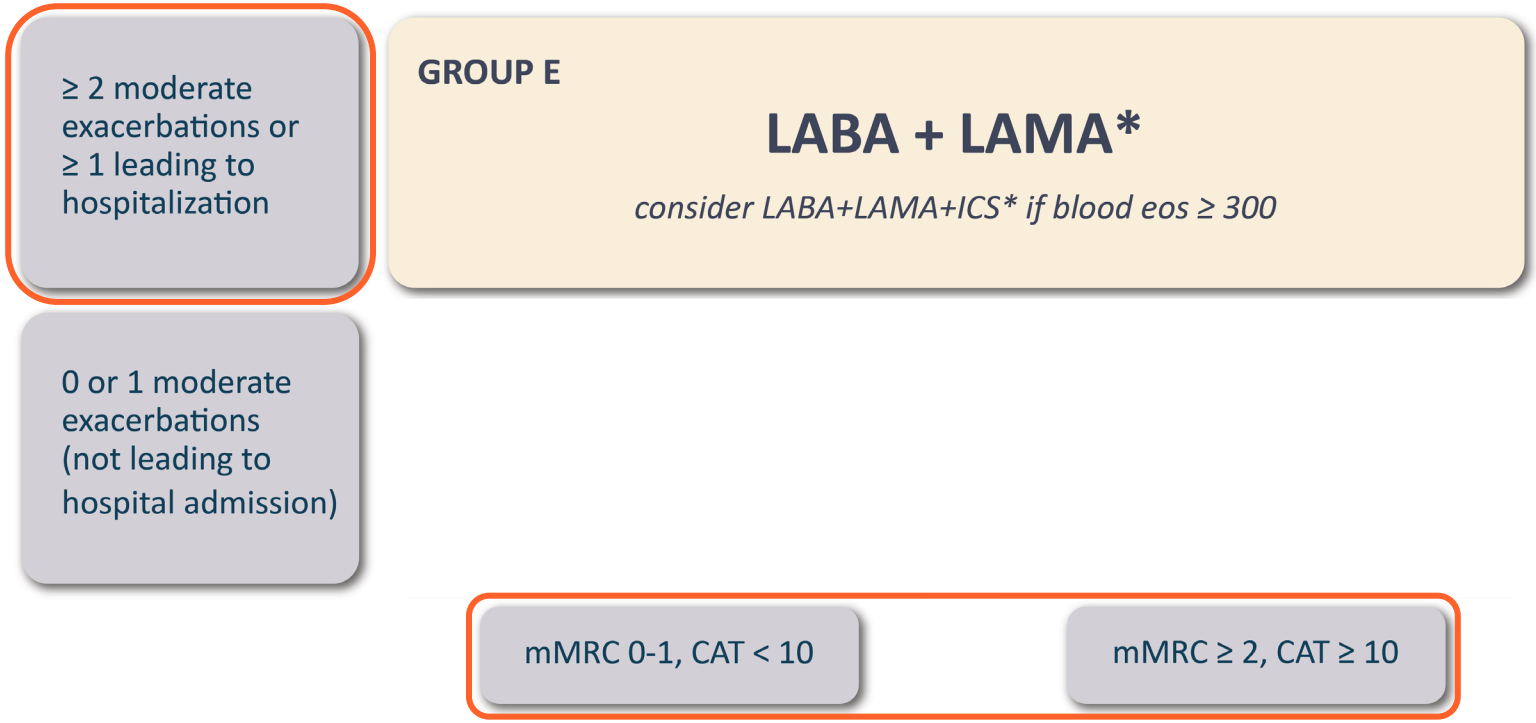


*Single inhaler therapy may be more convenient and effective than multiple inhalers; single inhalers improve adherence to treatment

Exacerbations refers to the number of exacerbations per year; eos: blood eosinophil count in cells per microliter; mMRC: modified Medical Research Council dyspnea questionnaire; CAT™: COPD Assessment Test™.

Initial Pharmacological Treatment

Figure 3.7



*Single inhaler therapy may be more convenient and effective than multiple inhalers; single inhalers improve adherence to treatment

Exacerbations refers to the number of exacerbations per year; eos: blood eosinophil count in cells per microliter; mMRC: modified Medical Research Council dyspnea questionnaire; CAT™: COPD Assessment Test™.

LABA + LAMA is the recommended initial therapy for most patients with COPD.

LAMA/LABA combinations are first-line therapy for most COPD patients!

umeclidinium/vilanterol
(Anoro)
- *Dry powder inhaler*
- ***Once daily***

glycopyrrolate/ indacaterol
(Utibron)
- *Capsule DPI*
- *Twice daily*

tiotropium/olodaterol
(Stiolto)
- *Soft mist inhaler*
- ***Once daily***

glycopyrrolate/ formoterol
(Bevespi)
- HFA MDI
- Twice daily

Little head-to-head efficacy data - **consider delivery device, pt preference, cost**

Appropriate inhaled medication choice considerations

- Availability, coverage, and OOP cost
- Patient beliefs, perception, and preferences
- Consider cognition, dexterity, and strength

 **Dry powder inhaler**	Requires a forceful, deep inhalation
 **Metered-dose inhaler**	Requires coordination between triggering and inhalation. Consider spacer/VHC.
 **Soft mist inhaler**	Requires coordination (less) and slow inhalation
 **Nebulizer**	Consider for patients unable to use other methods

Which COPD patients should be on inhaled steroids?

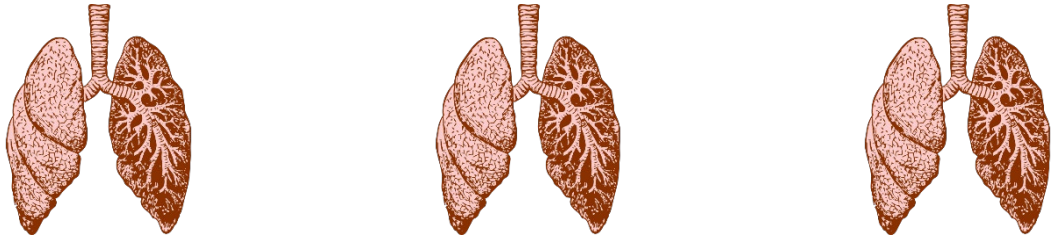
ICS in COPD:
Known adverse drug effects

Side-effect	Cohort studies	Population-based case-control studies	Randomized con-trolled trials	Systematic reviews and meta-analysis
Pneumonia	+	+	+	+
Tuberculosis	+	+		+
Non-tuberculous mycobacterial pulmon-ary diseases		+		
Diabetes	+	+		+
Bone fracture	+	+		+
Cataract	+	+		+
Peptic ulcer hemorrhages		+		
Local reactions (oral candidiasis, dysphonia)	+	+	+	+
Skin bruising	+		+	+

Avdeev, Sergey et al. “Withdrawal of inhaled corticosteroids in COPD patients: rationale and algorithms.” *International journal of chronic obstructive pulmonary disease* vol. 14 1267-1280. 10 Jun. 2019, doi:10.2147/COPD.S207775

ICS in COPD:
Low-value ICS care causes harm and increases utilization

- Difference in absolute risk for PNA in FLAME: 1.8%
- Number needed to harm (NNH): ~66
- Optum COPD patients receiving inappropriate ICS: ~350,000

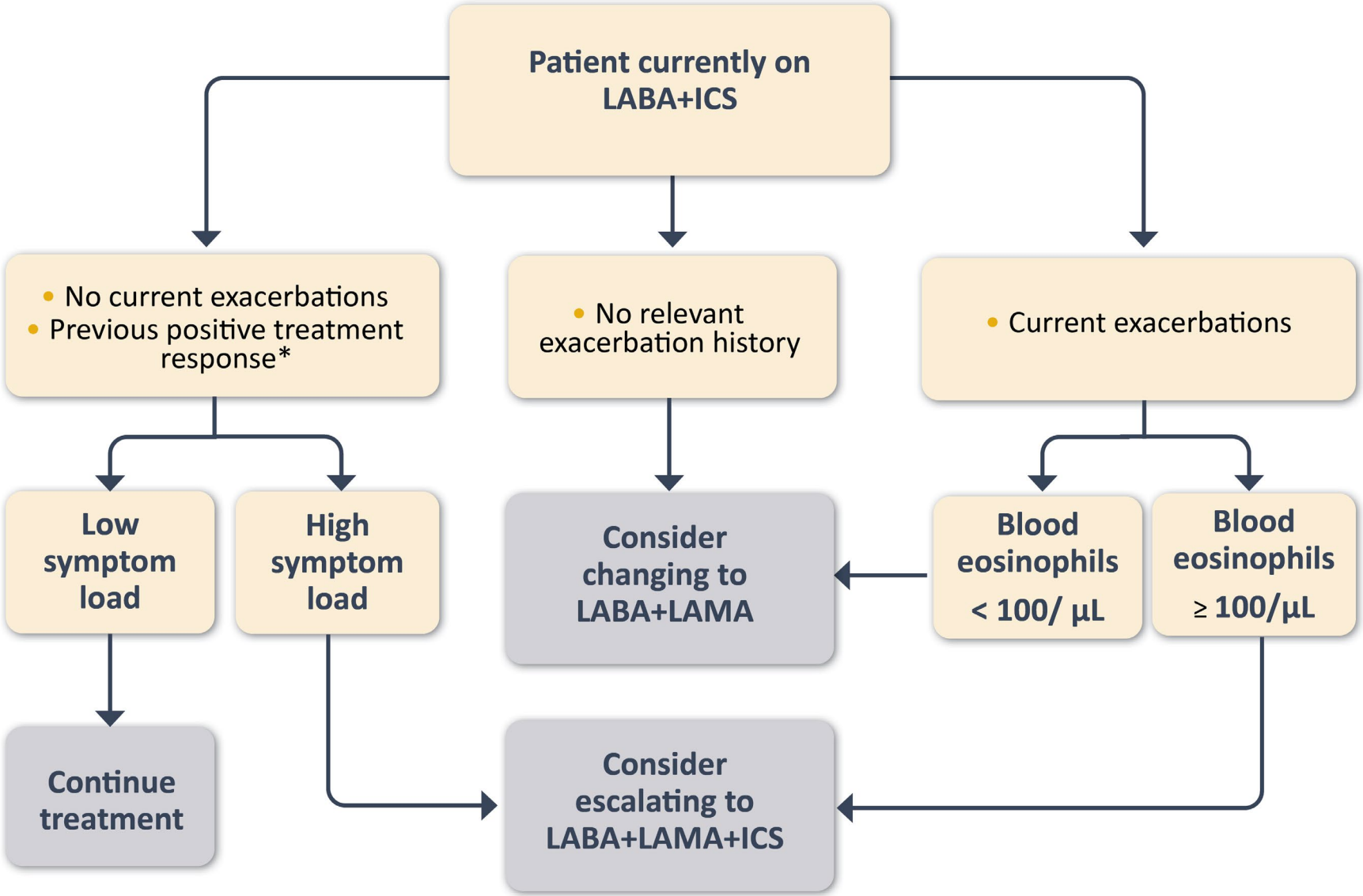


>5,000 Optum COPD patients may be hospitalized for pneumonias attributable to inappropriate ICS use annually!

FLAME: Wedzicha et al, N Engl J Med 2016; 374:2222-2234

(All numbers estimated!)

What to do with patients that are already on LABA+ICS?



*Patient previously had exacerbations and responded to LABA+ICS treatment

Decoding lab report / peripheral eosinophilia

	Test	Result
	WBC	5.8 x10E3/uL
	RBC	4.35 x10E6/uL
	Hemoglobin	13.1 g/dL
	Hematocrit	39.1 %
	MCV	90 fL
	Lymphs	30 %
	Platelets	224 x10E3/uL
	Immature Grans (Abs)	0.0 x10E3/uL
	Eos (Absolute)	**0.9 x10E3/uL**
	Baso (Absolute)	0.1 x10E3/uL
	MCH	30.1 pg
	MCHC	33.5 g/dL
	Neutrophils	47 %
	Immature Granulocytes	0 %
	Monocytes	7 %
	Eos	15 %
	Basos	1 %
	Neutrophils (Absolute)	2.7 x10E3/uL
	Lymphs (Absolute)	1.8 x10E3/uL
	Monocytes(Absolute)	0.4 x10E3/uL
	RDW	13.9 %

- CBC with manual diff
- Absolute eosinophil count
- Looking for **>300** cells per uL.
- %Eos can be helpful but may not flag as abnormal.

0.9 x 10E3/uL = 0.9 x 0.001
Need to multiply by 1000 to get to cells per uL

(This patient's absolute eosinophil count is **900** – likely to be an ICS responder)

ICS in COPD: Summary

- ICS use is associated with increased risk for pneumonia.
- This risk is outweighed by benefit of decreased exacerbations in only a small subset of COPD patients:
  - Concomitant asthma
  - Peripheral eosinophils >300/uL
  - More than exacerbation annually
- ICS can be safely discontinued without taper in most pts.

Restrict ICS use in COPD to patients with eosinophilia and/or frequent exacerbations.
Stop ICS in patients that are unlikely to benefit.

Will newly approved medications help my COPD patients?

Ensifentrine – new maintenance therapy option

- Inhaled selective dual phosphodiesterase-3 (PDE3) and phosphodiesterase-4 (PDE4) inhibitor
  - Bronchodilator and anti-inflammatory effects
  - Delivered via standard jet nebulizer
  - US FDA approved (June 2024) for treatment of stable COPD
- Phase 3 trials (ENHANCE-1 and -2) demonstrated:
  - Effective bronchodilation, improved dyspnea
  - Good safety and tolerability
- Methodologic problems in these trials:
  - *LABA-LAMA treatment was not permitted in the trial*
  - *32-45% of participants were on no background therapy* for COPD

Not actual size.

Ensifentrine – cost effectiveness and conclusion

Population	Treatment	Comparator	Evidence Rating	Annual WAC	Health-Benefit Price Benchmark
Moderate-to-severe COPD	Ensifentrine	Maintenance therapy alone	B+	$35,400	$7,500 to $12,700

"COPD is a common cause of severe respiratory problems. Current evidence shows that ensifentrine decreases COPD exacerbations when used in combination with some current inhaled therapies, but there are uncertainties about how much benefit it may add to unstudied combinations of inhaled treatments. Unfortunately, the manufacturer chose a price for ensifentrine far above the value-based price. This may lead payers to implement formulary hurdles that could limit provider and patient access to this promising new treatment."

– ICER's Chief Medical Officer David Rind, MD

LONG-TERM COST EFFECTIVENESS

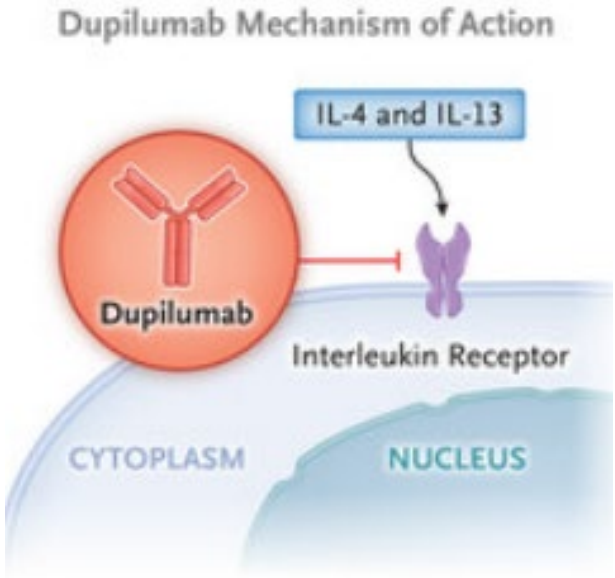
In cost-effectiveness analyses, ensifentrine results in fewer exacerbations and in greater QALYs, evLYs, and life years. At a wholesale acquisition cost of $35,400 per year, the incremental cost-effectiveness ratios for ensifentrine are $492,000 per QALY gained and $426,000 per evLY gained. Ensifentrine would meet commonly used cost-effectiveness thresholds at an annual price between $7,500 and $12,700. If ensifentrine is shown to increase the day-to-day quality of life of patients living with COPD, beyond quality of life improvements associated with fewer exacerbations, the cost-effectiveness would improve, but would continue to exceed commonly used cost-effectiveness thresholds at an annual price of $35,400.

Lin G, et al. Ensifentrine for the Treatment of Chronic Obstructive Pulmonary Disease: Effectiveness and Value. Institute for Clinical and Economic Review, July 16, 2024

GOLD: *"…the studies were not designed to assess the impact of ensifentrine on top of LABA+LAMA or LABA+LAMA+ICS making it difficult to fully position this agent in our treatment algorithm."*

Dupilumab – new therapy option for refractory COPD exacerbations

- Anti IL-4 and IL-13 monoclonal antibody
  - Subcutaneous injection every 14 days
  - US FDA approved (September 2024) for treatment of COPD in patients with *elevated blood eosinophils*

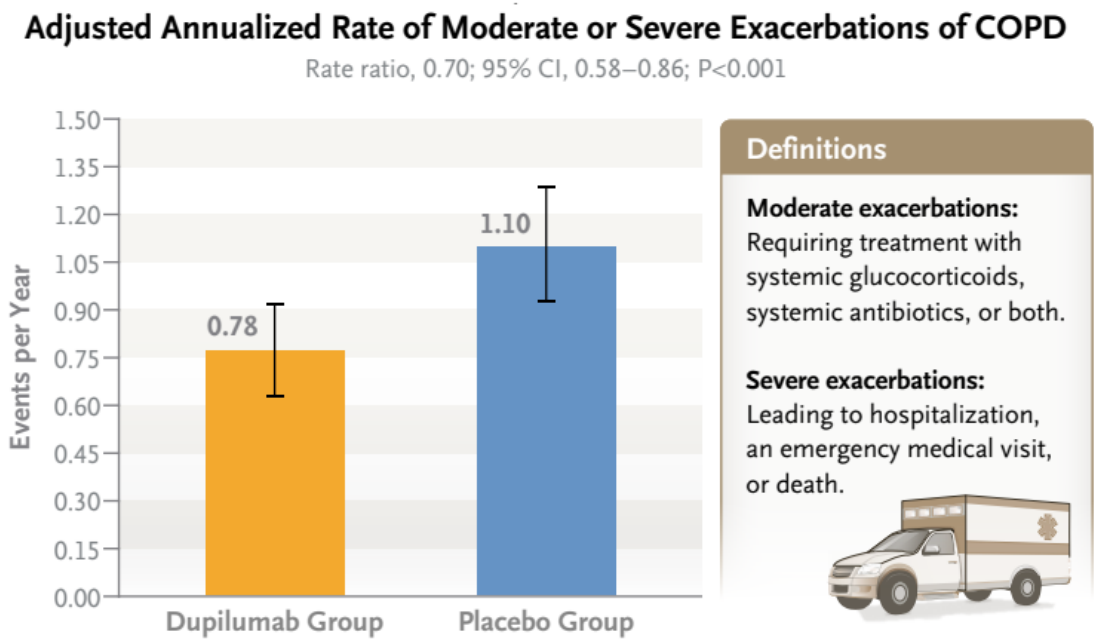


Dupilumab is also FDA-approved for:

- Atopic dermatitis
- Asthma
- CRSwNP
- Eosinophilic esophagitis
- Prurigo Nodularis

Dupilumab – evidence and role in COPD treatment

- Phase 3 trials (NOTUS and BOREAS):
  - In patients with recurrent exacerbations despite baseline LAMA/LABA/ICS and eos >300:
    - Reduced exacerbation rates 30-34%
    - Modest improvements in lung function and sx
    - Improvements sustained at 52 weeks
    - Adverse events similar to placebo



Dupilumab can be considered as an add-on therapy for patients with COPD and peripheral eosinophilia who continue to have exacerbations despite adherence to LAMA/LABA/ICS therapy.

What non-pharmacologic treatments will benefit my COPD patients?

Vaccination for Stable COPD

Figure 3.6

People with COPD should receive all recommended vaccinations in line with the relevant local guidelines:

- Yearly influenza vaccination **(Evidence B)**
- SARS-CoV-2 (COVID-19) vaccination based on WHO and CDC updated recommendations **(Evidence B)**
- Either one dose of 21-valent pneumococcal conjugate vaccine (PCV21) or one dose PCV20, as recommended by the CDC **(Evidence B)**. Pneumococcal vaccination has been shown to reduce the incidence of community-acquired pneumonia and exacerbations for people with COPD **(Evidence B)**
- Respiratory syncytial virus (RSV) vaccination for individuals aged ≥ 60 years and/or with chronic heart or lung disease, as recommended by the CDC **(Evidence A)**
- Tdap (dTaP/dTPa) vaccination to protect against pertussis (whooping cough) for people with COPD that were not vaccinated in adolescence, as recommended by the CDC **(Evidence B)**
- Zoster vaccine to protect against shingles for people with COPD aged > 50 years, as recommended by the CDC **(Evidence B)**

RSV and vaccination - facts

- RSV infection 4-10% of high-risk adults over 4-year period
- 14,000 global in-hospital deaths due to RSV

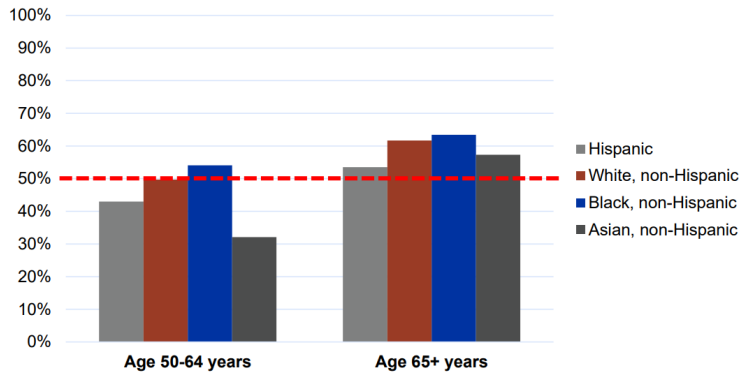
- Three FDA-approved RSV vaccines
- 2024 CDC recommended schedule:
  - All adults aged 75+
  - Adults aged 60-74 who are at increased risk for RSV disease
- **Vaccine efficacy is 94% vs RSV-related LRTI in year 1, 64% in year 2**
- Need for additional vaccine doses will be evaluated by ACIP in future

***Note: People can self–attest to the presence of a risk factor.* The following medical and other conditions increase the risk of severe RSV disease:**

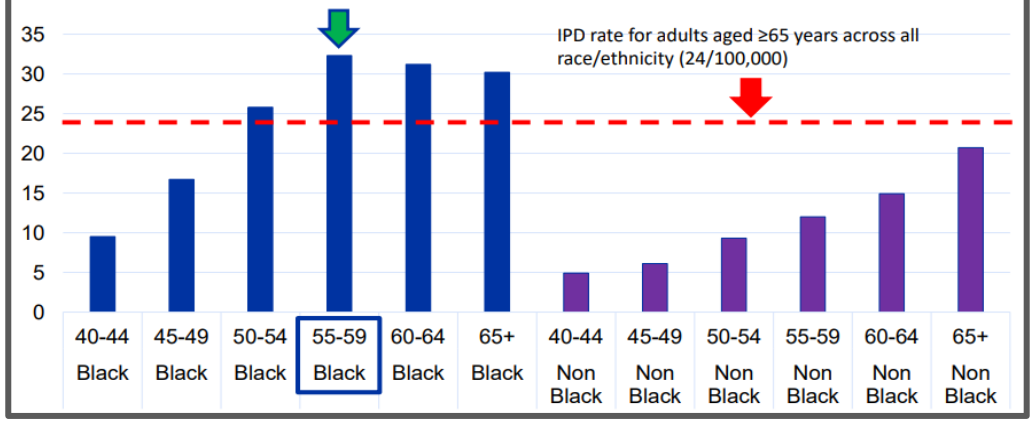
- Chronic cardiovascular disease e.g., heart failure, coronary artery disease, congenital heart disease. Excludes isolated hypertension.
- Chronic lung or respiratory disease e.g., chronic obstructive pulmonary disease, emphysema, asthma, interstitial lung disease, cystic fibrosis.
- End stage renal disease or dependence on hemodialysis or other renal replacement therapy.
- Diabetes mellitus complicated by chronic kidney disease, neuropathy, retinopathy, or other end–organ damage.
- Diabetes mellitus requiring treatment with insulin or sodium–glucose cotransporter 2 (SGLT2) inhibitor.
- Neurologic or neuromuscular conditions causing impaired airway clearance or respiratory muscle weakness e.g., post–stroke dysphagia, amyotrophic lateral sclerosis, muscular dystrophy. Excludes history of stroke without impaired airway clearance.
- Chronic liver disease e.g., cirrhosis
- Chronic hematologic conditions e.g., sickle cell disease, thalassemia
- Severe obesity (body mass index ≥ 40 kg/m2)
- Moderate or severe immune compromise
- Residence in a nursing home
- Other chronic medical conditions or risk factors that a health care provider determines would increase the risk of severe disease due to viral respiratory infection e.g., frailty, concern for presence of undiagnosed chronic medical conditions, residence in a remote or rural community where escalation of medical care is challenging.

ACIP: Pneumococcal Vaccine for PCV-naïve adults ≥50

About 32–54% of adults aged 50–64 years have underlying conditions with risk-based pneumococcal vaccine indication*



IPD rates (any pneumococcal serotype) in Black adults peak at a younger age compared with Non-Black adults



PCV-naïve adults (or adults with unknown history) DRAFT

Underlying conditions	Previous vaccination history	Age 19–49 years	Age ≥50 years
None	None	No vaccine recommendation	PCV21 OR PCV20 OR PCV15 → ≥1yr → PPSV23*
Chronic medical conditions	None	PCV21 OR PCV20 OR PCV15 → ≥8wks† → ≥1yr → PPSV23*	
CSF leak, cochlear implant	None		
Immuno-compromised	None		

*If adults previously received PPSV23 before receiving a dose of PCV15, it need not be followed by another dose of PPSV23
†A minimum interval of 8 weeks can be considered for adults with an immunocompromising condition, cochlear implant, or cerebrospinal fluid leak

Use of 21-Valent Pneumococcal Conjugate Vaccine Among U.S. Adults: Recommendations of the Advisory Committee on Immunization Practices — United States, 2024 | MMWR

56

- ***ACIP recommends a pneumococcal conjugate vaccine (PCV) for all PCV-naïve adults aged ≥50***
- This recommendation was adopted by the CDC Director on October 23, 2024 and is now official.

Optum Health Education™

https://www.cdc.gov/acip/vaccine-recommendations/index.html

https://www.cdc.gov/acip/downloads/slides-2024-10-23-24/04-Kobayashi-Pneumococcal-508.pdf

Less frequently addressed, but impactful, vaccines for COPD patients

Herpes Zoster (Shingles)	• Risk of developing herpes zoster is 50% to 200% higher in people with COPD • 25% of COPD pts with HZ get worsening of respiratory symptoms • **Vaccine is highly efficacious (>90% protection)** • Only 31.6% of eligible adults have received the VZ vaccinations
Pertussis	• COPD patients have 3x risk of pertussis with complications • Exacerbation rate elevated 30 days before and after pertussis dx, and **remains elevated ~180 days after diagnosis**

Simon S, Joean O, Welte T, Rademacher J. The role of vaccination in COPD: influenza, SARS-CoV-2, pneumococcus, pertussis, RSV and varicella zoster virus. Eur Respir Rev. 2023;32(169):230034. doi:10.1183/16000617.0034-2023

Increased Burden of Pertussis Among Adolescents and Adults With Asthma or COPD in the United States, 2007 to 2019. Naeger, Sarah et al. CHEST, Volume 165, Issue 6, 1352 - 1361

Practical recs for increasing vaccination rates

- **Raise awareness** — know vaccine recommendations for your patient groups.
  - Familiarize all patient care team members with ACIP adult vaccine recommendations and how to share that information with patients with chronic respiratory conditions.

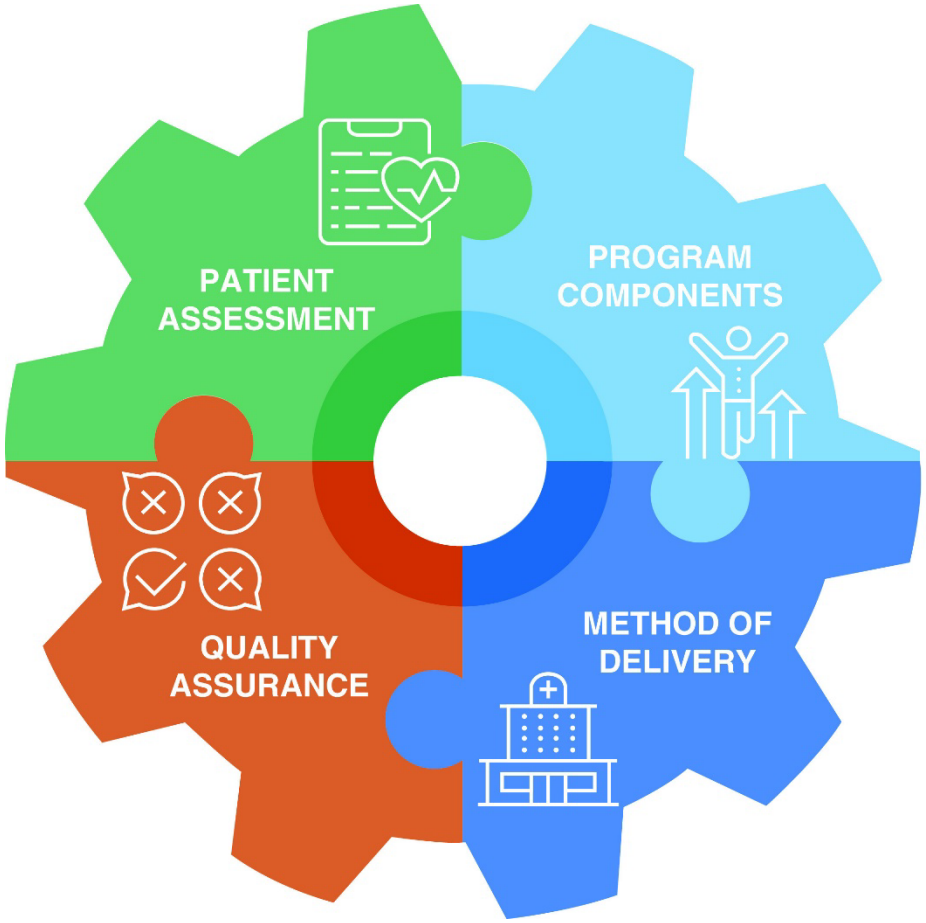
- **Co-administer vaccines** — improves overall rates.
  - Both the Tdap and shingles vaccines can be co-administered with the annual influenza and COVID-19 vaccines.

- **Provide clear instructions** on where to get vaccines.
  - If your clinic does not administer the vaccines, recommend **specific** locations.
  - Community pharmacies are underutilized.

- **Give strong recommendations**—recommendations from trusted clinicians improve rates.
  - Significant improvements in vaccine uptake followed messages that were clear and supportive—"Today you are due for your first shingles vaccine (or your 10-year Tdap booster) and your annual flu shot. We can give these at the end of your visit today"

Comprehensive care of adults with respiratory diseases must include vaccines. Yawn, Barbara P. et al. Annals of Allergy, Asthma & Immunology, Volume 131, Issue 3, 292 - 293

What is pulmonary rehabilitation?



ESSENTIAL COMPONENTS OF PULMONARY REHABILITATION

1. An initial center-based assessment by a health care professional
2. An exercise test at the time of assessment
3. A field exercise test
4. Quality of life measure
5. Dyspnea assessment
6. Nutritional status evaluation
7. Occupational status evaluation

8. Endurance training
9. Resistance training

10. An exercise program that is individually prescribed
11. An exercise program that is individually progressed
12. Team includes a health care professional with experience in exercise prescription and progression

13. Health care professionals are trained to deliver the components of the model that is deployed

Defining Modern Pulmonary Rehabilitation. Ann Am Thorac Soc. 2021 May; 18(5): e12–e29.

Pulmonary rehabilitation: benefits

Exercise capacity and Lung function	• 43 meters longer on 6 minute walk [1] • 7 watts higher on cycle ergometer [1] • Slower decline in FEV1 over 3 years [2]
Quality of life	• Clinically significant improvements in dyspnea, fatigue, emotional function, and mastery [3]
Health care utilization	• Decreased hospital days • Mixed studies on readmission rates [4]
Mortality	• PR enrollment within 90 days of hospital D/C for AECOPD *associated with* lower 1 year mortality (19.6% vs 7.3%)

Benefits are not permanent! Exercise capacity, symptoms, and HRQoL return to pre-rehab values after ~12 months. Pulmonary rehab maintenance programs may help benefits persist 12-24 mos.

Pulmonary rehab is PROFOUNDLY UNDERUTILIZED

Patients aren't aware
Most COPD patients have never heard of pulmonary rehab (ATS 2018)

Doctors don't refer
Only 3-16% of eligible patients referred, across multiple countries
<3% of Medicare patients referred to a pulmonary rehabilitation program within 12 months of hospitalization for COPD exacerbation
Non-Hispanic white patient referral **double** that of black patients
Barriers: low knowledge of PR, low knowledge of referral process

Patients don't complete
Many patients do not complete prescribed PR **(attrition rates ~60%)** Strong predictors of attrition: White race, current smoking, low functional capacity, low neighborhood SDI

Pulmonary rehab in COPD: Summary

- Pulmonary rehab programs are:
  - Highly effective at improving health-related quality of life and health care utilization in COPD patients
  - Highly cost-effective
  - Profoundly underutilized

- PCPs have a role as advocates and educators for PR

Learn about pulmonary rehab resources in your area

Refer symptomatic COPD patients for pulmonary rehab and encourage participation

Do patients with borderline hypoxemia need oxygen?

Which patients need oxygen therapy?

Patients with:

- Resting SpO2 <89%, or
- Resting SpO2 <90% + cor pulmonale or HCT>55%

Long-term oxygen therapy (LTOT) is indicated!

- **Improves mortality!**
- **Probably QOL improvements**
- **Target 15+ hours per day**

Patients with:

- Moderate hypoxemia (SpO2 89-93%)
- Hypoxemia only with exertion

- **No difference in mortality**
- **No difference in time to first hospitalization**
- **No difference in COPD exacerbations**
- **No difference in quality of life or 6 min walk**

Long-Term Oxygen Treatment Trial Research Group, Albert RK, Au DH, et al. A Randomized Trial of Long-Term Oxygen for COPD with Moderate Desaturation. *N Engl J Med*. 2016;375(17):1617-1627. doi:10.1056/NEJMoa1604344

Key points to remember

- Make sure your patients with “COPD” have had spirometry
- LAMA/LABA is an appropriate initial therapy for symptomatic COPD
- Get patients without exacerbations or eosinophilia off inhaled steroids
- Look for opportunities for improving your vaccination recommendation routine
- Refer symptomatic COPD patients for pulm rehab and encourage participation
- Mild or exertional hypoxemia does not require supplemental oxygen